

Application No. 10/088,966

Reply to Office Action

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*REMARKS/ARGUMENTS**The Pending Claims*

Claims 86, 88, 89, 92-94, 97, 100, 105, and 107 are pending, and are directed to methods to detect the taxonomic unit of any species of enterobacteria, but no species of another taxonomic unit.

*The Amendments to the Claims*

The claims have been amended to point out more particularly and claim more distinctly the present invention. In particular, claims 86, 92, and 105 have been amended to recite detection of DNA of any species of the taxonomic unit of Enterobacteriaceae, and no species of another taxonomic unit. This amendment is supported by the specification at, e.g., page 10, lines 19-23, page 25, lines 30-34, page 27, lines 15-22, and page 35, lines 9-24. Step (a) of each of claims 86, 92, 100, and 105 has been amended to recite that the nucleic acid molecules *consist of* at least one or a combination of SEQ ID NO: 2 and SEQ ID NO: 78. Each of claims 86, 92, 100, and 105 also has been amended to recite nucleic acid molecules which exhibit at least 90% identity with SEQ ID NO: 2 and/or SEQ ID NO: 78. This amendment is supported by the specification at, e.g., page 5, lines 20-21, and page 29, lines 27-28. Claims 86, 92, 100, and 105 have further been amended to delete reference to nucleic acid molecules which hybridize specifically with SEQ ID NO: 2 and/or SEQ ID NO: 78. Claims 86 and 100 have been amended to recite, as a method step, that any species of the taxonomic unit of Enterobacteriaceae, and no species of another taxonomic unit, is detected by the formation of the hybrid nucleic acids. This amendment is supported by the specification at, e.g., page 10, lines 19-23, page 25, lines 30-34, page 27, lines 15-22, and page 35, lines 9-24. Claims 92 and 105 have been amended to delete the term "genera." Certain claims also have been amended to correct grammar or matters of form. Claims 96 and 102 have been cancelled. Accordingly, no new matter has been added by way of these amendments.

*The Office Action*

The Office Action rejects claims 86, 88, 89, 92, 93, 94, 96, 97, 100, 102, 105, and 107 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. The Office

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Action rejects claims 86, 88, 89, 92-94, 96-98, 102, 105, and 107 under 35 U.S.C. § 103 (a) as allegedly unpatentable over U.S. Patent 5,654,141 (Mariani et al.) ("the Mariani patent") in view of Yamamoto et al. (GenBank Accession Number AB001341, submitted January 25, 1997). Reconsideration of these rejections is hereby requested.

*Discussion of Rejection Under 35 U.S.C. § 112, First Paragraph*

The Office Action rejects claims 86, 88, 89, 92, 93, 94, 96, 97, 100, 102, 105, and 107 under Section 112, first paragraph, as allegedly lacking written description. In essence, the Office Action argues that the present application does not adequately describe the genus of nucleic acid sequences that exhibit 70% identity or 90% identity to SEQ ID NO: 2 and SEQ ID NO: 78. This rejection is traversed for the reasons set forth below.

Applicants note that claims 86, 92, 100, and 105 have been amended to recite nucleic acid molecules which exhibit at least 90% identity with SEQ ID NO: 2 and/or SEQ ID NO: 78. According to the Office Action, the present application expressly describes only SEQ ID NO: 2 and SEQ ID NO: 78, and not the "hundreds" of nucleic acid sequences that are complements of or have 70% or 90% identity to SEQ ID NO: 2 and/or SEQ ID NO: 78. Thus, the Office Action concludes that the specification does not disclose a representative number of species of the claimed genus.

Contrary to the assertion of the Office Action, the genus of nucleic acid sequences that are 90% identical to SEQ ID NO: 2 does not contain "hundreds" of species. In this respect, SEQ ID NO: 2 is 20 nucleotides in length. A sequence that is 90% identical to a 20 nucleotide sequence can contain, at most, 2 mismatched nucleotides. Using a stochastic calculation for determining combinations, Applicants determined that the number of nucleic acid molecules sharing 90% identity with a 20 nucleotide target sequence such as SEQ ID NO: 2 is only 190. Accordingly, the genus of nucleic acid molecules encompassed by SEQ ID NO: 2 is not as large as alleged by the Office Action.

The written description requirement is satisfied by the disclosure of sufficiently detailed, relevant identifying characteristics of a chemical or biological material, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and

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structure, or some combination of such characteristics. See *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.3d 956, 969-70, 63 U.S.P.Q. 2d 1609, 1617 (Fed. Cir. 2002). At the time the subject application was filed, it was well known that primer sequences of 20 nucleotides (e.g., SEQ ID NO: 2) to 30 nucleotides (e.g., SEQ ID NO: 78) could be modified so as to generate variant sequences of similar efficiency. For example, Christopherson et al., *Nucleic Acid Research*, 25: 654-658 (1997) (enclosed herewith), discloses the effects of internal primer template mismatches on the efficiency of reverse transcription and PCR amplification. As outlined in the abstract, the presence of two to four mismatches in a sequence of 30 nucleotides (i.e., sequences that share 93% and 86% identity, respectively, with the normal primer) in primer template duplexes does not have a significant effect on RT-PCR. However, the presence of five or six mismatches (i.e., sequences that share less than 85% identity with the normal primer) reduces the PCR product yield by 22 to 100-fold, respectively, relative to the homogenous template.

Accordingly, as evidenced by the Christopherson reference, nucleic acid sequences that share at least 90% identity with SEQ ID NO: 2 and/or SEQ ID NO: 78 are capable of amplifying DNA targets with the same efficiency as SEQ ID NO: 2 and/or SEQ ID NO: 78. Given the disclosed structure of SEQ ID NOs: 2 and 78 coupled with the disclosed function, one of ordinary skill in the art reading the present application would have been readily apprised of the possible variations in the sequence of SEQ ID NOs: 2 and 78 that would yield a nucleic acid molecule with at least 90% sequence identity to SEQ ID NOs: 2 and 78 and retain the functional characteristics SEQ ID NOs: 2 and 78. In other words, one of ordinary skill in the art would have understood that Applicants had possession of nucleic acid sequences that have at least 90% identity to a nucleic acid molecule consisting of SEQ ID NO: 2 and/or SEQ ID NO: 78. Thus, the written description requirement is satisfied with respect to claims 86, 92, 100, and 105.

This situation is in distinct contrast with *The Regents of the University of California vs. Eli Lilly & Co.* 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997) (see Office Action at page 3). Based on the disclosure of the subject application and the knowledge in the art, one of ordinary skill in the art would appreciate not only the function of sequences at least 90% identical to SEQ